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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
|---|---|---|---|
| 09/012,369 | 01/23/98 | MARGOLIS B | 231/198 |

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HM12/0120

| EXAMINER | |
|---|---|
| EYLER, Y | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | 12 |

**DATE MAILED:** 01/20/00

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

# Office Action Summary

| Application No. | Applicant(s) |
|---|---|
| 09/012,369 | Margolis et al. |
| **Examiner** | **Group Art Unit** |
| Yvonne Eyler | 1642 |

☒ Responsive to communication(s) filed on *Nov 2, 1999*.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

**Disposition of Claims**

☒ Claim(s) *1-12 and 19-25* is/are pending in the application.

Of the above, claim(s) *5-9, 11, 12, and 19* is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-4, 10, and 20-25* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119**

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

**Attachment(s)**

☐ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *4*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

*--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---*

## DETAILED ACTION

### *Election/Restriction*

1. Applicant's election with traverse of species (a) Cancers and neoplasms in Paper No. 11 is acknowledged. The traversal is on the ground(s) that it would not require undue burden to search and consider because all the diseases have in common an abnormality in signal transduction. This is not found persuasive because each disease type is not the result of identical abnormalities in signal transduction and each type of abnormality requires unique considerations and searches.

The requirement is still deemed proper and is therefore made FINAL.

Claims 1-4, 10 and 20-25 will be examined in light of the election of species of cancers and neoplasms in the instant paper no. 11 and agents which bind to APB domains in paper no. 9. Claims 5-9 11, 12, and 19 are withdrawn from consideration as being to a non-elected invention. Claims 20-25 will be examined only in as much as they depend from claim 4.

### *Claim Rejections - 35 USC § 112*

2. Claims 1-4, 10, and 20-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is vague and indefinite in the recitation of a "disease or disorder in an organism characterized by an abnormality in a signal transduction pathway. The metes and bounds of the

encompassed diseases or disorders cannot be determined. It is not clear what comprises an "abnormality" in a signal transduction pathway. The specification at page 7 describes an abnormality in a signal transduction pathway to be realized by an "abnormality" in cell growth, migration, or "other function." There is no definition of what is considered to be an "abnormality" in cell growth or migration versus what is not and there is not definition of what "other functions" are. The definition is circular, defining an "abnormality" in a signal transduction pathway by another "abnormality," neither of which can be identified without a definition of what is normal and what is abnormal. Further, the claim is drawn to an "abnormality" in "a" signal transduction pathway, of which there are many within a cell and even more within an organism, and it is not clear to which one the claims refer, or if the claims refer to a singular pathway or a malfunction all instances of a specific type of pathway. Further, claim 1 recites disrupting or promoting an "interaction" between an APB domain and it's binding partner which is vague and indefinite. It is not clear what actions define an "interaction."

Claim 2 is vague and indefinite in that the encompassed diseases or disorders cannot be determined. The diseases or disorders are defined as being characterized by APB binding, but what the APB is binding to or how it differs and defines a disease is not described such that the diseases or disorders encompassed can be determined. The specification recites on page 9 that the binding must accentuate or cause "to some extent", the disease or disorder which information is not found to adequately define the diseases encompassed since the "extent" of accentuation of "what?" cannot be determined. Claim 2 is further vague and indefinite in the recitation of "a

therapeutic amount" without a definable functional limitation. The specification at page 8 defines a therapeutic amount as that amount inhibiting "to some extent" cell proliferation or growth or having a therapeutic effect in a human. The outcome that is considered "therapeutic" is not provided such that one could identify it, nor is the "extent" definitive of the outcome provided.

Claim 2 further refers to an "APB recognition region" present in a protein, which region cannot be determined. There is no information supplied regarding the characteristics defining an APB recognition region such that a protein having one may be identified. This applies also to the "amino acid region able to bind to an APB domain" as recited in claim 10.

Claim 3 refers to "one or more activities" of a receptor tyrosine kinase for which the metes and bounds cannot be determined. There is no definition of what actions comprise a definitive activity of the RTK and what actions do not such that one of skill would be able to determine if the appropriate activities are decreased commensurate in scope with the claimed invention.

Claim 4 recites a Markush group from which the receptor tyrosine kinase is selected from which group contains a member which is not a receptor tyrosine kinase. EGF is not a receptor, EGFR is.

Claim 24 lacks antecedent basis for TRK since the receptor listed in claim 4 is TRKA.

3. Claims 1-4, 10, and 20-25 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman,* (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands,* 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

In light of the elected invention, the claims are drawn to and being examined with regard to the therapeutic treatment of cancer or neoplasms by administration of an agent which binds to an APB domain.

The specification discloses the discovery of a here-to-fore unknown binding by a region within the N-terminus of Shc to autophosphorylated EGFR, HER-2, or TRKA.

There is insufficient objective evidence provided to support a role for Shc APB binding (or any other APB protein binding) in the mediation of signal transduction or in the onset and development of cancer. There is no objective evidence provided that disruption or promotion of Shc APB binding to EGFR, HER-2, TRKA or any other APB-receptor interactions results in the predictable remediation of symptoms of cancer. No therapeutic agents which disrupt or promote such binding are provided, including any agents which bind to the APB domain. Indeed, the region of the EGFR receptor to which the APB domain of Shc binds is not identified. Neither is the role, if any, of the binding in signal transduction provided. Indeed, the specification teaches that it is art-known that specific binding is determined by SH2 domains and that the physiological

role of APB binding is unknown (see page 57 and page 64 of the instant specification). Further, the specification warns that the data presented must be approached with caution and that the interactions seen instantly, involving protein fragments, may not be representative of the full-length situation (see page 63).

Thus, in light of the unpredictability of the therapeutic role of modulation of Shc APB binding to signal transduction and cancer modulation, it would require undue experimentation for one of skill to practice the claimed invention without further guidance and evidence.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yvonne Eyler, Ph.D. whose telephone number is (703) 308-6564. The examiner can normally be reached on Monday through Friday from 830am to 630pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**paula.hutzell@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Yvonne Eyler, Ph.D.
Primary Examiner
January 18, 2000